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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/624,328	07/22/2003	John McMichael	13024/38627A	6971

4743 7590 06/25/2009

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EXAMINER	
HUGHES, ALICIA R	

ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
06/25/2009	PAPER

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte JOHN MCMICHAEL and KENNETH A. UNICE

Appeal 2009-002709[1]
Application 10/624,328
Technology Center 1600

Decided:[2] June 25, 2009

Before DONALD E. ADAMS, LORA M. GREEN, and
FRANCISCO C. PRATS, *Administrative Patent Judges*.

PRATS, *Administrative Patent Judge*.

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[1] The real party in interest is Milkhaus Laboratory, Inc.

[2] The two-month time period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, begins to run from the decided date shown on this page of the decision. The time period does not run from the Mail Date (paper delivery) or Notification Date (electronic delivery).

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to methods of alleviating symptoms of a psychological condition. The Examiner has entered two rejections for obviousness. We have jurisdiction under 35 U.S.C. § 6(b).

We affirm one obviousness rejection, but reverse the other.

STATEMENT OF THE CASE

Claims 1, 2, 4, 5, 8-18, and 20-24 are pending and on appeal (App. Br. 5). Claims 1 and 15, the independent claims, are representative and read as follows:

> 1. A method of alleviating symptoms of a psychological condition selected from the group consisting of depression, anxiety disorders, panic attacks, premenstrual dysphoric disorder (PMDD), and premenstrual syndrome (PMS) comprising administering to a subject in need thereof nerve growth factor in an amount effective to treat one or more symptoms of said psychological condition.
>
> 15. A method of alleviating symptoms of a psychological condition selected from the group consisting of sleep disorders, tension headaches, and constipation comprising administering to a patient in need thereof nerve growth factor in an amount effective to treat one or more said symptoms.

The Examiner cites the following documents as evidence of unpatentability:

Siuciak	US 5,599,560	Feb. 4, 1997
Frey, II et al.	US 2003/0072793 A1	Apr. 17, 2003

THE MERCK MANUAL OF DIAGNOSIS AND THERAPY, 1525-1539, 1932-1933 (Mark H. Beers, M.D., & Robert Berkow, M.D., eds., 17th ed. 1999).

The following rejections are before us for review:

Claims 1, 2, 4, 5, 8-18, and 20-24 stand rejected under 35 U.S.C. § 103(a) as being obvious in view of Frey and The Merck Manual (Ans. 4-7).

Claims 1, 2, 4, 5, 11-15, and 20-24 stand rejected under 35 U.S.C. § 103(a) as being obvious in view of Siuciak and The Merck Manual (Ans. 7-10).

OBVIOUSNESS -- FREY AND THE MERCK MANUAL

ISSUE

The Examiner cites Frey as teaching "the administration of nerve growth factor ['NGF'] for the treatment of disorders or diseases of the central nervous system (Paragraphs 50, 51, and 169)" (Ans. 4). The Examiner notes that Frey lists nerve growth factor among its preferred neurologic agents, and teaches "the treatment of central nervous system disorders, particularly affective disorders and anxiety disorders (Paragraph 169)" (*id.* at 4-5).

The Examiner cites The Merck Manual as teaching that depression "falls under a broad class of mood or affective disorders (Page 1525)," that "individuals with mixed anxiety-depression possess conditions of symptoms that have both anxiety and depression (page 1529)," and that "a patient with the condition of premenstrual syndrome ['PMS'] is characterized, *inter alia*, by anxiety and depression (page 1932)" (*id.* at 5).

The Examiner urges that although Frey is "silent to the use of NGF to treat the psychological conditions of PMS, anxiety disorders, and panic attacks, Frey . . . do[es] in fact teach and provide the artisan with the necessary motivation to use nerve growth factor in the treatment of affective

and anxiety disorders (Paragraph 169)" (*id.*). Based on the references' teachings, the Examiner finds that an ordinary artisan would have recognized that treating depression and anxiety "would also be treating and alleviating the symptoms of related conditions and ailments that have depression and anxiety as symptoms, namely anxiety disorders, PMS, and depression associated with menustration [sic] and anxiety associated with panic attacks, most especially in view of the teaching of the Merck Manual" (*id.*). Thus, the Examiner concludes, "Frey . . . in view of the Merck Manual make obvious the claimed subject matter" (*id.* at 6).

Appellants contend that Frey "discloses a laundry list of more than forty (40) potential agents for delivery to the CNS of a subject by a particular mode of drug administration, but fails to disclose or suggest that any one of the forty-plus agents disclosed therein is for the treatment of any one disorder" (App. Br. 10). Rather, Appellants urge, "most of the forty-plus agents listed would not be expected to be therapeutic for most of the seventeen or more conditions listed in paragraph [0169]" (*id.*).

For example, Appellants argue, an ordinary artisan "would not expect that an 'anti-cancer agent' (Frey II, paragraph [0045]) would be therapeutic for an anxiety disorder (Frey II, paragraph [0169]). Similarly, one would not expect that cisplatin, an anti-viral agent, (Frey II, paragraph [0043]) would be therapeutic for attention deficit disorder (Frey II, paragraph [0169])" (*id.*).

Thus, Appellants contend, because Frey does not "specifically correlate any particular agent as a therapeutic for a specific disorder, one of skill in the art would not know which of the many agents disclosed in Frey . . . could be used for the treatment of, for example, affective disorders" (*id.* at 11). Therefore, Appellants argue, "one of skill in the art would not be

motivated upon review of Frey II to use NGF for the treatment of any disorder, much less the psychological disorders or symptoms recited in independent claims 1 and 15, respectively" (*id.*).

Appellants further contend that The Merck Manual does not remedy Frey's shortcomings because it does not mention the use of NGF in treating any neurological disorder (*id.*). Thus, Appellants argue, "the combined disclosure of Frey II and Beers fails to disclose or suggest the claimed invention. Accordingly, there can be no *prima facie* case of obviousness" (*id.*).

In view of the positions advanced by Appellants and the Examiner, the issue with respect to this rejection is whether Appellants have shown that the Examiner failed to make a prima facie case that a person of ordinary skill in the art would have been prompted by the cited references to administer nerve growth factor to a patient in order to treat the disorders recited in claims 1 and 15.

FINDINGS OF FACT ("FF")

1. Claim 1 recites a method in which nerve growth factor is administered to alleviate symptoms of a psychological condition. The nerve growth factor is administered to alleviate symptoms of depression, anxiety disorders, panic attacks, premenstrual dysphoric disorder (PMDD), or premenstrual syndrome (PMS).

2. Claim 15 also recites a method in which nerve growth factor is administered to alleviate symptoms of a psychological condition. The nerve growth factor is administered to alleviate sleep disorders, tension headaches, or constipation.

3. Frey discloses "a method for transporting or delivering an agent to a central nervous system of a subject. The method employs administration of the agent to a tissue outside the subject's nasal cavity and innervated by the trigeminal nerve" (Frey [0006]).

For example, "[i]n one embodiment, the method administers the agent through the mucosa or epithelium of the tongue, mouth, skin, or conjunctiva. In another embodiment, the method includes administering a composition of the agent under the tongue, to the skin, or to the conjunctiva of the subject" (*id.*).

4. Frey discloses that its methods are advantageous in that "[a]dministration of agents by the method of the invention can more effectively deliver the agent to the CNS, brain and/or spinal cord, can decrease the amount of agent administered outside the CNS, brain and/or spinal cord, and, preferably, can decrease the undesirable systemic effects of the agent" (Frey [0039]).

5. Frey discloses:

> The present method can administer a variety of different agents to the central nervous system. In general, the method of the invention can administer an agent that can be employed for diagnosis, prevention, or treatment of a disease or disorder affecting the CNS, brain, and/or spinal cord; that can nourish or maintain a cell or tissue in the CNS, brain, and/or spinal cord; that can prevent or inhibit degradation of a cell or tissue in the CNS, brain, and/or spinal cord; that can alter gene expression in a cell or tissue in the CNS, brain, and/or spinal cord; that can regulate a functional activity of a cell or tissue in the CNS, brain, and/or spinal cord; that can regulate growth of a cell or tissue in the CNS, brain, and/or spinal cord; or the like.

(Frey [0037].)

6. Frey discloses that the "agent can be an organic pharmaceutical, an inorganic molecule, a peptide, a peptoid, a protein, a lipid, or carbohydrate, a nucleic acid, or the like" (Frey [0041]). According to Frey:

> An organic pharmaceutical can be a stimulant, a sedative, an hypnotic, an analgesic, an anticonvulsant, an antihypertensive, an antiemetic, an anxiolytic, an antidepressant, a tranquilizer, a cognition enhancer, a narcotic antagonist or agonist, a vitamin or nutrient, an enzyme inhibitor, an antioxidant, a free radical scavenger, a metal chelating agent, an agent which can alter the activity of an ion channel, an antineoplastic, an anti-inflammatory, or a combination thereof. Advantageously, an organic pharmaceutical modulates a functional activity of an enzyme, receptor, cell, or tissue in the CNS, brain, and/or spinal cord. A preferred agent that can regulate a functional activity includes, for example, a neurotransmitter, a neuromodulator, a nootropic, a receptor agonist or antagonist, or a combination thereof.

(*Id.* at [0042].)

7. Frey also discloses:

> The organic pharmaceutical can be an antiviral, an antibacterial, an antiparasitic, an antifungal, or a combination thereof. Preferred agents for diagnosis, prevention or treatment of an infection of the CNS, brain, and/or spinal cord include an antibacterial, an antiparasitic, and/or an antifungal agent. Preferred antiviral agents include agents that stop or inhibit the replication or spread of viruses such as adenoviruses, arboviruses, enteroviruses, rabies viruses, and HIV.

(Frey [0043].)

8. Frey discloses that an "inorganic agent can be an antioxidant or an anti-cancer agent (e.g. cisplatin)" [0045].

9. Frey discloses:

> Neurologic agents are one preferred category of agents that can be administered according the present invention. A neurologic agent employed in the method of the present invention can be any substance that promotes the function or survival of neurons and prevents the loss or further loss of nerve cells. For example, a preferred neurologic agent can promote nerve or glial cell growth, promote survival of functioning cells, augment the activity of functioning cells, enhance the synthesis of neurotransmitter substances, augment the activity of naturally occurring nerve growth promoting factors, act as a nerve growth promoting factor, prevent degeneration of neurons, induce regrowth of dendrite and axon, have more than one of these properties, or the like. A preferred neurologic agent is a neurotrophic and/or neuritogenic factor that is similar to a naturally occurring nerve growth promoting substance. Numerous of such neurologic agents are known to those of skill in the art.

(Frey [0050].)

10. Frey discloses:

> Among the preferred neurologic agents are proteins, growth factors, and neurotrophins such as nerve growth factor (NGF), neurotrophins 3, 4, and/or 5 (NT-3, NT-4 and/or NT-5), brain-derived neurotrophic factor (BDNF), fibroblast growth factors (FGFs, e.g., basic fibroblast growth factor), insulin, insulin-like growth factors (IGFs, e.g., IGF-I and/or IGF-II), ciliary neurotrophic factor (CNTF), glia-derived neurotrophic factor (GDNF), glia-derived nexin, combinations thereof, and the like.

(Frey [0051].)

11. Frey discloses that "[n]erve growth factor [NGF] stimulates mitosis and growth processes associated with cell, particularly nerve cell, development" (Frey [0097]). Also, the "biological activities of NGF include increasing levels of choline acetyl transferase" (*id.* at [0099]).

12. Frey discloses that a "preferred embodiment of the present composition includes an effective amount of NGF with a pharmaceutically-acceptable liquid carrier containing an appropriate amount of micelles included of GM-1 ganglioside. GM-1 is thought to act synergistically with nerve growth factor (NGF) to protect neurons and promote nerve regeneration and repair" (Frey [0134]).

13. Frey discloses:

> The present method can be employed to deliver agents to the brain for diagnosis, treatment or prevention of disorders or diseases of the CNS, brain, and/or spinal cord. These disorders can be neurologic or psychiatric disorders. These disorders or diseases include brain diseases such as Alzheimer's disease, Parkinson's disease, Lewy body dementia, multiple sclerosis, epilepsy, cerebellar ataxia, progressive supranuclear palsy, amyotrophic lateral sclerosis, affective disorders, anxiety disorders, obsessive compulsive disorders, personality disorders, attention deficit disorder, attention deficit hyperactivity disorder, Tourette Syndrome, Tay Sachs, Nieman Pick, and other lipid storage and genetic brain diseases and/or schizophrenia. The method can also be employed in subjects suffering from or at risk for nerve damage from cerebrovascular disorders such as stroke in the brain or spinal cord, from CNS infections including meningitis and HIV, from tumors of the brain and spinal cord, or from a prion disease. The method can also be employed to deliver agents to counter CNS disorders resulting from ordinary aging (e.g., anosmia or loss of the general chemical sense), brain injury, or spinal cord injury.

(Frey [0169].)

14. The Merck Manual discloses that depression can include symptoms of anxiety (*see, e.g.* Merck Manual 1529 (Table 189-2)). The Merck Manual also discloses that Premenstrual syndrome can include symptoms of depression (*id.* at 1932).

PRINCIPLES OF LAW

In *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 415 (2007) the Supreme Court rejected a "rigid approach" to the analysis under 35 U.S.C. § 103, and instead emphasized that, "[t]hroughout this Court's engagement with the question of obviousness, our cases have set forth an expansive and flexible approach . . . ." The Court also noted, however, that

> [I]t can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements *in the way the claimed new invention does* . . . because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known.

Id. at 418-419 (emphasis added); *see also id.* at 418 (requiring a determination of "whether there was an apparent reason to combine the known elements *in the fashion claimed* by the patent at issue") (emphasis added).

The court advised that in determining whether the prior art supplied a reason for practicing the claimed subject matter, the analysis "need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *Id.* at 418; *see also id.* at 421 ("A person of ordinary skill is . . . a person of ordinary creativity, not an automaton.").

The Court further advised, however, that "rejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, *there must be some articulated reasoning* with some rational underpinning to

support the legal conclusion of obviousness." *Id.* at 418 (quoting *In re Kahn*, 441 F.3d 977, 988, (Fed. Cir. 2006) (emphasis added).

In *KSR*, the Supreme Court also addressed the "obvious to try" issue:

> When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103.

Id. at 421.

Thus, as our reviewing court has stated, "[o]bviousness does not require absolute predictability of success. . . . For obviousness under § 103, all that is required is a reasonable expectation of success." *In re O'Farrell*, 853 F.2d 894, 903-04 (Fed. Cir. 1988).

> [T]o have a reasonable expectation of success, one must be motivated to do more than merely to "vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful." Similarly, prior art fails to provide the requisite "reasonable expectation" of success where it teaches merely to pursue a "general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it."

Medichem S.A. v. Rolabo S.L., 437 F.3d 1157, 1165 (Fed. Cir. 2006) (quoting *O'Farrell*, 853 F.2d at 903-04).

ANALYSIS

We agree with Appellants that the Examiner did not make a prima facie case of obviousness with respect to claims 1 and 15.

Frey discloses that administering CNS-acting therapeutic agents to tissue innervated by the trigeminal nerve is advantageous in that the agents are more effectively delivered to the CNS and less drug is delivered outside the CNS, thus decreasing undesirable systemic side effects (FF 3-4). Frey discloses that a number of different types of drugs, with widely varying chemical makeups and therapeutic properties, are amenable to the disclosed administration techniques (FF 6-7). NGF is among the preferred agents deliverable by Frey's techniques (FF 10).

Frey also discloses that its administration techniques can be used to treat a wide variety of neurological disorders, ranging from psychological disorders, such as affective and anxiety disorders, to actual physical damage, such as caused by stroke, viral or bacterial infection, or from tumors (Frey [0169] (FF 13)). However, while the Examiner urges that paragraph [0169] discloses treating anxiety disorders with NGF, that paragraph simply sets forth a list of disorders that are amenable to the disclosed treatment methods, and does not explicitly state which of the many and varied therapeutic agents listed should be used to treat those disorders (*see* FF 13).

Given the extensive variety of therapeutic agents amenable to its techniques (FF 6-7), combined with the wide variety of treatable disorders and diseases with vastly different etiologies (FF 13), we do not agree with the Examiner that a person of ordinary skill in the art would have considered the lists in Frey as amounting to a disclosure that any of the cited drugs were useful in treating any of the named ingredients. Rather, in our view, an

ordinary artisan would have viewed Frey as simply providing separate lists of the disorders and drugs amenable to its techniques.

We therefore do not agree with the Examiner that a person of ordinary skill in the art would have been prompted by Frey to treat anxiety disorders with NGF. Nor do we agree with the Examiner that Frey would have provided an ordinary artisan with a reasonable expectation that all of the drugs listed would be useful in treating anxiety disorders.

We note that Frey discloses that NGF stimulates nerve cell growth and development, increases choline acetyl transferase, and can be used to protect neurons and promote nerve regeneration and repair (FF 11-12). However, the Examiner has not explained how any of these activities would have led a person of ordinary skill in the art to treat the disorders recited in claims 1 and 15 with nerve growth factor.

As noted above, "rejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, *there must be some articulated reasoning* with some rational underpinning to support the legal conclusion of obviousness." *KSR*, 550 U.S. at 418 (quoting *In re Kahn*, 441 F.3d at 988 (emphasis added)).

Thus, we agree with Appellants that Frey does not disclose, or suggest with sufficient specificity, using nerve growth factor to treat depression, anxiety disorders, panic attacks, premenstrual dysphoric disorder (PMDD), or premenstrual syndrome (PMS) as recited in claim 1, or sleep disorders, tension headaches, or constipation as recited in claim 15. We also agree with Appellants that The Merck Manual does not remedy Frey's shortcomings in this respect. We therefore reverse the Examiner's rejection

of claims 1 and 15, and their dependent claims, as obvious over Frey and The Merck Manual.

OBVIOUSNESS -- SIUCIAK AND THE MERCK MANUAL

ISSUE

Claims 1, 2, 4, 5, 11-15, and 20-24 stand rejected under 35 U.S.C. § 103(a) as being obvious in view of Siuciak and The Merck Manual (Ans. 7-10).

The Examiner cites Siuciak as teaching that "it is known in the art that nerve growth factor (Col. 6, lines 16-31) is used for the treatment of depression as well as panic disorders (Col. 6, lines 44- 65)" (*id.* at 7). As in the previous rejection, the Examiner cites The Merck Manual as teaching that depression "falls under a broad class of mood or affective disorders (Page 1525)," that "individuals with mixed anxiety-depression possess conditions of symptoms that have both anxiety and depression (page 1529)," and that "a patient with the condition of premenstrual syndrome ['PMS'] is characterized, *inter alia*, by anxiety and depression (page 1932)" (*id.* at 7-8).

The Examiner urges that although Siuciak is "silent to the use of NGF to treat the psychological conditions of PMS, anxiety disorders, and panic attacks, Siuciak does in fact teach and provide the artisan with the necessary motivation to use nerve growth factor in the treatment of affective and anxiety disorders (Col. 6, lines 44-65)" (*id.* at 8). Based on the references' teachings, the Examiner finds that an ordinary artisan would have recognized that treating depression and anxiety "would also be treating and alleviating the symptoms of related conditions and ailments that have depression and anxiety as symptoms, namely anxiety disorders, PMS, and depression associated with menustration [sic] and anxiety associated with

panic attacks, most especially in view of the teaching of the Merck Manual" (*id.*). Thus, the Examiner concludes, "Siucuak [sic] in view of the Merck Manual make obvious the claimed subject matter" (*id.* at 8).

Appellants contend that the Examiner's conclusion of obviousness is erroneous because "NGF is a different protein with different properties than BDNF, NT-3 and NT- 4 disclosed by Siuciak for treatment of depression" (App. Br. 12). In fact, Appellants argue, "Siuciak itself emphasizes that NGF lacks some of the biological properties of BDNF, NT-3 and NT-4 (col. 3, lines 11-14) contradicting the Examiner's apparent assertion that all members of the neurotrophin family can be used interchangeably" (*id.*; *see also* Reply Br. 5). In support of the proposition that NGF has different biological properties than BDNF, NT-3, and NT-4, Appellants cite the Friedman[3] article (App. Br. 12; *see also* 21 (Appendix B (Exhibit C))).

Because NGF has different properties than other members of the neurotrophin family, Appellants argue, an ordinary artisan "would not have concluded from Siuciak that NGF could be used as a therapeutic in disorders normally treated with BDNF, NT-3 or NT-4 and would not be motivated upon review of Siuciak to use NGF to alleviate the symptoms of the psychological disorders or any other disease" (App. Br. 12). Appellants argue that The Merck Manual fails to remedy Siuciak's shortcomings in this regard (*id*).

Thus, Appellants urge, the Examiner's conclusion of obviousness is based on hindsight reasoning, and the Examiner therefore "has failed to

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[3] W.J. Friedman et al., *Differential Actions of Neurotrophins in the Locus Coeruleus and Basal Forebrain*, 119 EXPERIMENTAL NEUROLOGY 72-78 (1993).

establish a *prima facie* case of obviousness for the subject matter of any of [the] claims" (*id.* at 13).

Appellants do not argue the claims subject to this ground of rejection separately. We select claim 1 as representative of the rejected claims. *See* 37 C.F.R. § 41.37(c)(1)(vii).

In view of the positions advanced by Appellants and the Examiner, the issue with respect to this rejection is whether Appellants have shown that the Examiner erred in finding that an ordinary artisan would have been prompted by the teachings of Siuciak and The Merck Manual to administer nerve growth factor to alleviate symptoms of depression, anxiety disorders, panic attacks, premenstrual dysphoric disorder (PMDD), or premenstrual syndrome (PMS), as recited in claim 1.

FINDINGS OF FACT

15. Siuciak discloses a "method for treating depression which involves the use of neurotrophic factors, specifically the NGF family of neurotrophins. Although not wishing to be bound by theory, these neurotrophins are believed to be active for the treatment of depression based on their ability to alter serotonin turnover in the brain" (Siuciak, col. 4, ll. 16-22).

16. Siuciak discloses that "animal models used to predict the antidepressant activity of test agents indicate that neurotrophins that alter serotonin levels appear to have such activity" (Siuciak, col. 4, ll. 28-31).

17. Siuciak discloses:

> One group of compounds that have recently been found to be active in altering serotonin turnover in the brain are the neurotrophins. The neurotrophin family includes brain-derived neurotrophic factor (BDNF), neurotrophin-3 (NT-3) and

> neurotrophin-4 (NT-4), all of which have recently been molecularly cloned and shown to be members of the nerve growth factor (NGF) family by virtue of their sequence homology.

(Siuciak, col. 2, ll. 47-55.)

18. Siuciak discloses:

> Studies involving the in vivo actions of the neurotrophins, in particular the neurotrophin BDNF, have confirmed their actions in maintaining the survival and regulating the function or phenotype of various neuronal cells. . . . A recent report described the in vitro survival effect of NT-3 and NT-4 (but not NGF) on locus ceruleus neurons (Friedman, et al. Exp. Neurol 119: 72-78 (1993).

(Siuciak, col. 2, l. 66, through col. 3, l. 14.)

19. Siuciak discloses that "[i]n a preferred embodiment of the invention, BDNF and/or NT-3 are delivered into the midbrain tegmentum, near the periaqueductal gray and the dorsal raphe, areas of the brain which contain an abundance of serotonergic neurons. In a preferred embodiment, the neurotrophin BDNF is used to reduce depression" (Siuciak, col. 5, ll. 6-11).

20. Friedman discloses a study comparing "different neurotrophins in the regulation of neuronal survival and function using dissociated embryonic cell cultures from two brain regions, the basal forebrain (BF) and locus coeruleus (LC)" (Friedman 72 (abstract)).

21. Friedman found that "[s]pecific neurotrophins such as NT-3 and NT-4 enhanced survival of both neuronal populations. NGF, which has no effect on LC neurons, influenced the BF by increasing cholinergic function but not survival, in contrast to BDNF, NT-3, and NT-4" (Friedman 76).

22. Friedman discloses that NGF, BDNF, NT-3, and NT-4 all increased choline acetyl transferase in BF cells (Friedman 72 (abstract)).

23. Friedman concluded that the "discovery that neuronal survival in both the basal forebrain and locus coeruleus is affected by common target-derived trophic factors provides a possible mechanism by which these distinct populations undergo necrosis in a single degenerative disorder such as Alzheimer's disease" (Friedman 76-77).

PRINCIPLES OF LAW

It is well settled that, "in a section 103 inquiry, 'the fact that a specific [embodiment] is taught to be preferred is not controlling, since all disclosures of the prior art, including unpreferred embodiments, must be considered.'" *Merck & Co. Inc. v. Biocraft Laboratories, Inc.*, 874 F.2d 804, 807 (Fed. Cir. 1989) (quoting *In re Lamberti*, 545 F.2d 747, 750 (CCPA 1976)); *see also In re Mills*, 470 F.2d 649, 651 (CCPA 1972) ("All the disclosures in a reference must be evaluated, including nonpreferred embodiments, and a reference is not limited to the disclosure of specific working examples." (citations omitted)).

ANALYSIS

Appellants' arguments do not persuade us that the Examiner erred in finding that an ordinary artisan would have been prompted by Siuciak and The Merck Manual to administer nerve growth factor to alleviate symptoms of depression, anxiety disorders, panic attacks, premenstrual dysphoric disorder (PMDD), or premenstrual syndrome (PMS), as recited in claim 1.

We note that Siuciak discloses BDNF and NT-3 as being the preferred members of the NGF family for treating depression (FF 19). However, as noted above, a reference must be evaluated for all it teaches, not just its

preferred embodiments. *See Merck v. Biocraft*, 874 F.2d at 807; *see also In re Mills*, 470 F.2d 649, 651.

Thus, in the instant case, Siuciak explicitly discloses that members of the NGF family are useful in treating depression (FF 15). Given this teaching, we agree with the Examiner that a person of ordinary skill in the art would have reasoned that any of the proteins in the related NGF family (FF 17) would have been suitable to treat the disorder.

We further note that Siuciak and Friedman provide evidence that unlike NT-3 and BDNF, NGF does not promote survival of certain neuronal populations (*see* FF 18, 21). However, Appellants fail to point to any specific scientific principle suggesting that NGF's failure to promote neuronal survival would have led an ordinary artisan to consider it unsuitable as a treatment for depression despite Siuciak's generic disclosure.

Moreover, Friedman discloses that NGF shares with NT-3 and BDNF the capacity to increase choline acetyl transferase activity in certain neuronal populations (FF 22). Siuciak also notes that the preferred agents, BDNF and NT-3, share sequence homology with other members of the NGF family of proteins (FF 17). Thus, while NGF may be different from other members of its family in some respects, it also shares properties with the other members, including Siuciak's preferred treatment agents.

Therefore, in contrast to the other appealed rejection, we do not agree with Appellants that Siuciak's generic disclosure amounts to an invitation to vary numerous parameters, try numerous possibilities, or follow a promising suggestion with only vague or general guidance. *See Medichem v. Rolabo*, 437 F.3d at 1165. Rather given Siuciak's generic disclosure of using NGF family members to treat depression, and the fact that the family is disclosed

as consisting of only a few related proteins (FF 17), the instant situation is more akin to that described in *KSR*:

> When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103.

KSR, 550 U.S. at 421. We again note that "[o]bviousness does not require absolute predictability of success. . . . For obviousness under § 103, all that is required is a reasonable expectation of success." *In re O'Farrell*, 853 F.2d at 903-04.

In sum, because we are not persuaded that the Examiner failed to make a prima facie case of obviousness with respect to claim 1, we affirm the Examiner's rejection of that claim as being obvious over Siuciak and The Merck Manual.

Claims 2, 4, 5, 11-15, and 20-24 fall with claim 1. *See* 37 C.F.R. § 41.37(c)(1)(vii).

SUMMARY

We reverse the Examiner's rejection of claims 1, 2, 4, 5, 8-18, and 20-24 under 35 U.S.C. § 103(a) as being obvious in view of Frey and The Merck Manual.

However, we affirm the Examiner's rejection of claims 1, 2, 4, 5, 11-15, and 20-24 under 35 U.S.C. § 103(a) as being obvious in view of Siuciak and The Merck Manual.

TIME PERIOD

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED-IN-PART

cdc

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